REMARKS

Claims 24-29, 39, 40, 44 and 45 are pending. Claim 28 is cancelled herein without prejudice, and claims 1-23, 30-38, 41-43, 46 and 47 were previously cancelled without prejudice. Claims 24-27, 29, 39, 40, 44 and 45 are proposed to be amended. The amendments add no new matter. New claims 48-51 are proposed herein. The new claims are supported throughout the specification and as discussed herein below.

Interview Summary:

At the outset, Applicants would like to thank Examiners Rooke and Carlson for the helpful telephone interview conducted on February 28, 2006. During the interview, amendments which focus the claims on peptides which stabilize the native conformation of target polypeptides were discussed, particularly with respect to distinguishing the prior art of record. The Examiners acknowledged that an isolated peptide of SEQ ID NO: 1 is not taught by Naumovski et al. After further discussion, the Examiners agreed to consider amendments set out herein as they further distinguish the prior art of record.

Objection to the Title:

The Office Action objects to the title of the application, stating that "the title as currently presented does not reflect the essence of the invention." Applicants have amended the title herein to "Peptide Molecules For Conformational Stabilization Of Polypeptides." The amendment adds no new matter.

Rejection under 35 U.S.C. §112, Second Paragraph:

The indefiniteness rejection of claim 24 under 35 U.S.C. §112, second paragraph is maintained over the phrase "natural binding partner." While Applicants continue to disagree as to the indefiniteness of the phrase, the rejection is rendered moot by the amendments to claim 24 proposed herein, which remove the phrase. Withdrawal of the rejection is respectfully requested.

Rejections under 35 U.S.C. §102:

Naumovski et al.

Claims 24-29, 44 and 45 are rejected under 35 U.S.C. §102(b) as anticipated by Naumovski et al. The Office Action states:

> Naumovski et al. teach the structure of Bcl2-binding protein ("Bbp") that specifically interacts with p53 protein in vivo, where the Bbp necessary requires for its binding to the p53 a specific ankyrin repeats and SH3 domain. See Figure 1, page 3886. Figure 3, page 3887 shows binding of Bbp protein to p53. (Claims 24, 25, and 44).
>
> Figure 6, page 3888, shows an amino acid sequence of Bbp, which contains REDEDEIEW amino acid sequence, as part of the SH3 domain necessary for binding of the Bbp protein to p53. The REDEDEIEW amino acid sequence of Bbp protein is identical to the instant invention (Claims 27 and 45).
>
> Therefore, the claims are anticipated by Naumovski et al. because the REDEDEIEW amino acid fragment of Bbp protein is identical to Claims 27 and 45 of the instant invention, and the amino acid fragment has the same function of binding p53 domain.

Applicants respectfully disagree.

Claim 24 is proposed to be amended to recite the following:

> "An isolated peptide which binds to and stabilizes the native conformation of a first polypeptide, but not a denatured conformation of the first polypeptide, in which the peptide comprises a fragment of a second polypeptide, said fragment comprising 600 amino acids or fewer of said second polypeptide, and binds to a site of the first polypeptide which at least partially overlaps a functional site of the first polypeptide."

Peptides that stabilize the native conformation of polypeptides are described throughout the specification, but particularly at, for example, page 3, lines 3-4, page 22, lines 5-8, page 28, line 4 to page 29, line 12, page 33, line 22 to page 36, line 2, and in the Examples and Table 1. Support for the language regarding a "fragment of a second polypeptide" is found, for example, at page 4, lines 10-11. Support for the language "comprising 600 amino acids or fewer" is found at page 28, lines 5-6. The "native conformation" language is supported at, for example, page 18, lines 9-15, which states in part that "A polypeptide in a 'native state' may include a conformation which corresponds to the conformation of a wild-type polypeptide."

The Naumovski et al. reference does not anticipate claim 24 as proposed to be amended. First, although the Naumovski et al. reference describes the binding of 53BP2 to p53, the reference does not teach that the 53BP2 polypeptide binds to and stabilizes the native conformation of the p53 polypeptide. It is not a fair assumption that binding of a polypeptide to another necessarily stabilizes the native conformation of either polypeptide. To the contrary, many binding interactions impose a conformational change on one or both polypeptides, rather than stabilizing a native conformation.

Second, the Naumovski et al. reference does not teach a fragment "comprising 600 amino acids or fewer" of the 53BP2 polypeptide that binds to any conformational state of the target p53 polypeptide, let alone that binds and stabilizes the native conformation of the p53 polypeptide. As such, this element of claim 24 as proposed to be amended is not satisfied and the amended claim is not anticipated by the Naumovski et al. reference. Reconsideration and withdrawal of the §102 rejection over Naumovski et al. is respectfully requested.

Kopchick et al.

Claim 24 is rejected under 35 U.S.C. §102(b) as anticipated by Kopchick et al. (U.S. 5,681,809). The Office Action states that "Kopchick et al. teaches growth hormone receptor antagonists," further stating:

> "The GH antagonist is considered to be a stabilizing agent, which binds to the GH polypeptide functional site. See column 5, line 37-43, and Abstract.
>
> Applicants state that while the reference teaches stabilization of a GH alpha helix by mutation, the reference does not teach that it is a GH mutant that binds to and stabilizes an alpha helix of a GH molecule, as would be required for this reference to anticipate claim 24.
>
> Examiner respectfully disagrees and stands by the rejection because claim 24 as written is anticipated by the reference because the antagonist stabilizes the receptor."

Applicants respectfully disagree.

First, the statement that "[t]he GH antagonist is considered to be a stabilizing

agent, which binds to the GH polypeptide functional site," appears to refer to intramolecular binding of the GH mutant to itself. This is not what is described in the reference. There is no teaching that the GH mutant polypeptides bind to themselves intramolecularly, or, for that matter, to each other. Nonetheless, claim 24 as proposed to be amended is clear in the requirement for two separate molecules – 1) "an isolated peptide" (i.e., one separate molecule) that binds to and stabilizes the native conformation of 2) "a first polypeptide" (another separate molecule). Thus, on its face, the claim as amended does not permit the "isolated peptide" to be the same as the "first polypeptide." The amended claim is even more explicit when it states that "the peptide comprises a fragment of a second polypeptide." That is, the claimed isolated peptide is not even a fragment of the recited first polypeptide.

Second, the proposed amendment makes it clear that the stabilizing referred to is "stabilization of the native conformation" of a polypeptide. There is no guarantee or even a predictable likelihood that binding of a ligand such as GH to a receptor such as the GH receptor stabilizes the native conformation of the receptor. Indeed, many such ligands function by inducing a conformational change in the receptor – i.e., by altering, rather than stabilizing, the conformation of the receptor in a manner that induces a change in signaling by the receptor. Thus, it is not proper to attempt to shift the burden to Applicants to show that it does not stabilize the native conformation of the receptor. In addition, this ligand/receptor stabilization argument appears to go counter to the previous argument in the Office Action that "the GH antagonist is considered to be a stabilizing agent that binds to the GH polypeptide functional site" – i.e., the intramolecular binding argument. One cannot rely on intramolecular binding and stabilization to satisfy one aspect of the claims and then turn to intermolecular characteristics to satisfy another aspect.

In view of the above, the Kopchick et al. reference fails to teach all elements of claim 24 as proposed to be amended. Reconsideration and withdrawal of the rejection is respectfully requested.

Winnacker et al.:

Claims 24, 28 and 29 are rejected under 35 U.S.C. §102(e) as being anticipated by Winnacker et al. (U.S. 6,451,541). The Office Action states:

> Winnacker et al. teach chaperones Hsp60 that bind to prion protein PrP^c. See Column 2, line 20-34. Also, Winnacker et al. teach that prior art chemical chaperones, such as glycerol, trimethylamine N-oxide, and DMSO stabilize PrP^c and prevent its conversion to PrP^{sc}. See column 3, line 16-24.
>
> Applicants state that the reference cannot anticipate the claimed invention because there is no teaching that any molecule among the "chemical chaperones" described in the reference binds to and stabilizes the native state of the polypeptide, but not a denatured state of the polypeptide.
>
> Examiner respectfully disagrees, because chemical chaperones stabilize the protein, as described above, and therefore claims 24, 28, and 29 as written are anticipated by the reference.

Applicants respectfully disagree.

First, claim 28 is cancelled herein, rendering the rejection moot with regard to that claim. Next, claim 24 as proposed to be amended requires the claimed composition to be a peptide. This excludes any non-peptide, chemical chaperones taught by Winnacker et al.

Further, claim 24 as proposed to be amended requires that the claimed peptide "comprises a fragment of a second polypeptide." Hsp60 molecules as taught by Winnacker to interact with PrP^c are full length Hsp60, rather than a fragment of Hsp60 as would be required to satisfy the limitations of the claims. As such, the molecules taught by the Winnacker et al. reference do not satisfy all elements of the claims. Reconsideration and withdrawal of the §102(e) rejection over Winnacker et al. is respectfully requested.

New claims:

New claims 48-51 are proposed to be added herein. New claim 48 requires a peptide that binds to and stabilizes the wild-type conformation of human p53, but not a mutant conformation of human p53, where the peptide fragment comprises 200 amino

acids or fewer. This new claim is supported throughout the specification, but particularly at, for example, page 6, lines 15-19 which relate to p53 as a target polypeptide for stabilization. Further support is found at page 28, lines 6-9, page 33, lines 22-23, in the Examples and in Table 1.

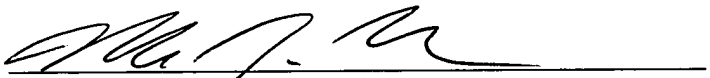
New claim 49 is supported in the specification at, for example, page 6, lines 20-21, in Table 1, and in the Examples. New claims 50 and 51 are supported in a similar manner.

In view of the above, the new claims 48-51 are fully supported in the specification and add no new matter.

In view of the above, all issues raised in the Office Action are addressed herein. Entry of the proposed amendments and reconsideration of the claims is respectfully requested.

Respectfully submitted,

Date: March 6, 2006



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